Case Report

Congenital leukemia diagnosed on day one of life - A rare entity: Case report

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Abstract

Congenital leukemia (CL) is a very rare disorder. Congenital leukemia is very uncommon myelo-proliferative disorder and may be associated with Down syndrome. Congenital Leukemia constitutes approximately 1% of all pediatric leukemias. Though rare, congenital leukemia (CL) is a condition readily recognized by pathologist, hemato-pathologists and pediatricians. Diagnosis can be made by the presence of leukemic cells in peripheral smear and bone marrow. Some cases of congenital leukemias have been reported with skin involvement presenting as reddish pink, light brown or purple papules or nodules and purpura. Congenital leukemia is a rare disorder, but it's a well-documented disease in which a disease process is detected at birth or very shortly within few days of birth. An estimated 160 to 190 reports of congenital leukemia has appeared in the literature. Most of the cases of CL diagnosed so far by various pathologists and hematopathologist belong to non-lymphoblastic lineage or myeloid lineage. Generally pediatric hematological malignancies are of lymphoid lineage. I have presented here a rare case of congenital leukemia of myeloid lineage which was diagnosed on day one in a low birth weight baby, born to non-consanguineous parents.

Key words

Congenital leukemia, Myeloid lineage, Down's syndrome, New born, Karyotyping, Translocation.

Introduction

Congenital leukemias are very rare and interesting group of hematologic malignancies that originate in utero and get diagnosed at delivery or within few days after delivery. Congenital leukemia (CL) is a rare condition that is usually diagnosed from birth to 6 weeks of life [1]. Its incidence is 1 in half a million live births and represents < 1% of all childhood leukemia [2, 3, 4]. These leukemias constitute approximately 0.8% of all childhood leukemias [5]. To call it as congenital leukemia some investigators and hematopathologists require specific symptoms or signs to be present at birth for the diagnosis of congenital leukemia.

According to Resnik, et al. and majority of the authors and hematopathologists the term congenital leukemia (CL) applies to those leukemias diagnosed within the first month of life [6]. According to Engel RK, et al.**,** the term congenital Leukemia should not be mixed with pediatric leukemias as congenital leukemias appear to have different natural histories, etiologies and different survival rates from other pediatric leukemias [7]. The diagnostic criteria used for CL are: a) disease presentation at or shortly after birth (within 30 days of birth), b) proliferation of immature/ presursor white cell population, c) infiltration of cells into extra-hemopoietic tissues and d) absence of congenital leukemia (CL) simulators [8]. The etiological considerations in CL include chromosomal defects, intrauterine and environmental reactions, viral pathogens and radiation exposure during pregnancy. Congenital Leukemia has also been reported in association with 21st Trisomy or Down's syndrome, Turner's syndrome, Klippel-Feil syndrome and Ellis-van Crevald syndrome [9]. Most notably, Down's syndrome is firmly established as a risk factor for leukemia [10]. Infants are much more likely to present with high leukocytes counts, hepatosplenomegaly and overt CNS disease [11, 12]. Here I have presented a case of congenital myeloid leukemia characterized by the presence of blasts and hyper leukocytosis on routine peripheral smear examination on day one. Karyotyping analysis showed double translocation of t[8;16] and t[17;19]). In view of low birth weight of the baby, parents did not agree to chemotherapy and patient was taken home against the medical advice. Infant died on Day 6.

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A term female infant weighing 2050 grams was delivered by normal vaginal delivery. Age of the mother was 26 years; she did not miss any ante natal checkups and all the antenatal visits were uneventful. Infant was a product of non-consanguineous marriage. Mother was a homemaker and has one living male child. Infant was kept under observation and blood was sent for routine investigations such as total bilirubin, complete blood picture (CBP) (**Figure - 1**). There was no maternal history of radiation exposure, no exposure to known teratogens, and no history of smoking or alcohol intake. On examination, there was mild hepato-splenomegaly. On peripheral smear, count was more than one lakh and predominant myeloblasts (**Figure - 2, 3, 4**). Platelet count was low. Further investigations were as per **Table - 1**.

Figure – 1: Clinical picture of newborn on Day 2.

Figure – 2: Microphotograph (Low power) showing leukocytosis, more at the tail end.

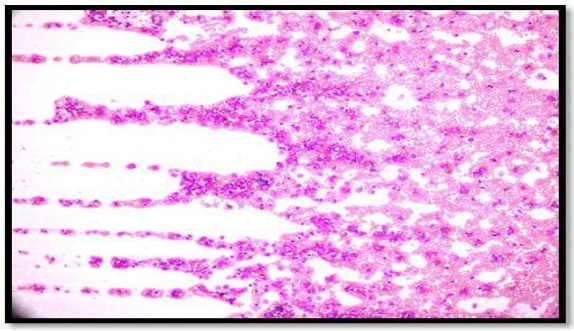
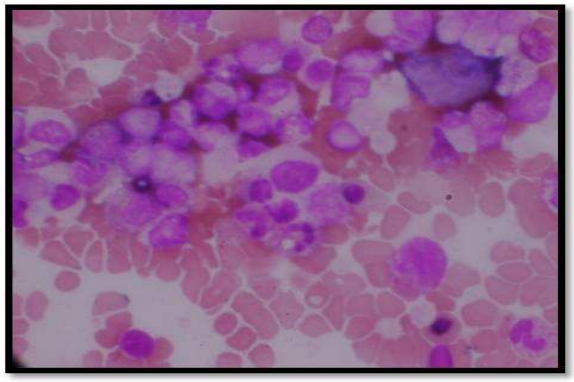


Figure – 3, 4: Micrphotographs (high power) showing myeloblasts and decreased platelets.



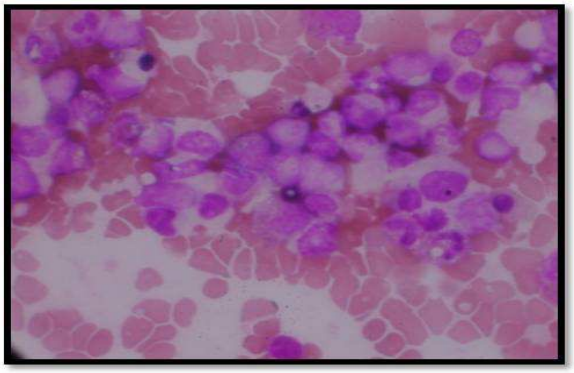


Table – 1: Investigations.

Investigation	**Results**
Hemoglobin	16.9 gm%
Red Blood Corpuscles	6.62 million /cu.mm
Hematocrit	51.2 Vol %
Total Leukocyte Count	**1,16,500 / cu.mm**
Differential count	
Blasts	68 %
Neutrophils	12 %
Metamyelocytes	08 %
Lymphocytes	06 %
Eosinophils	05%
Basophils	01 %
Platelet count	80,000 /cu.mm
t(8;16) Translocation	Positive
t(17;19) Translocation	Positive
Trisomy 21/ Down's syndrome	Negative
11q23 Translocation	Negative
USG –abdomen	Hepatosplenomegaly
Neonatal screening test	
Acylcarnitine profile	Normal
Amino Acid Profile	Normal
Glucose-6-Phosphate Dehydrogenase Defiency (G6PD)	Normal
Congenital Adrenal Hyperplasia(CAH)	Normal
Galactosemia(GAL)	Normal
Congenital Hypothyroidism (CH)	Normal
Biotinidase Deficiency (BIOT)	Normal
Cytochemistry	
Myeloperoxidase	Positive
Per-Iodic Acid Schiff	Negative

Discussion

The term congenital leukemia applies to cases of leukemia that are developed or diagnosed at birth, whereas the term neonatal and infantile leukemia were used to describe leukemia developing within the first one month of life or from one month to one year of life, respectively. Usually average time of diagnosis of congenital leukemia is from birth to six weeks of life. The criteria for diagnosis of CL are: a) disease presentation at or shortly after birth (within 30 days of birth), b) proliferation of immature/ presursor white cell population, c) infiltration of cells into extra-hemopoietic tissues and d) absence of congenital leukemia (CL) simulators [8]. Congenital leukemia simulators are the diseases that might cause leukemoid reactions leading to proliferation of immature cells. Congenital leukemia (CL) simulators include TORCH syndrome, hemolytic disease of the newborn (ABO or Rh incompatibility), hereditary spherocytosis, twin-twin transfusion, other neoplastic infiltrates (metastatic neuroblastoma, rhabdomyosarcoma, Langerhans cell histiocytosis) and the absence of 21st trisomy or Down's syndrome. Congenital leukemia (CL) is usually associated with mild to severe anemia and pallor, lethargy, mild to massive hepatosplenomegaly, sometimes involvement of the skin and leukocytosis. According to many authors and my extensive search of literature, most of the cases reported and published till date are associated with chromosomal anomalies like Down's syndrome. But in my case there are no features of Down's syndrome noted on examination of the neonate. It is very important to differentiate congenital leukemia from other abnormal hematological conditions which develop in response to various pathogens, hypoxemia and severe hemolysis in the neonates. Other differential diagnoses are congenital syphilis, intrauterine viral diseases, neuroblastoma and transient myeloproliferative syndrome associated with Down's syndrome. The exact causes of congenital leukemia are unknown, but according to Bayoumy, et al. congenital leukemia may be associated with

maternal exposure to radiation, maternal dietary exposure to bioflavonoid, maternal use of tobacco and illicit drugs, and inherited conditions, such as, Down's syndrome, neurofibromatosis, Bloom's syndrome and Fanconi's anemia [13]. Chromosomal instability is a hallmark of congenital leukemia, and the most common karyotypic abnormality involves the myeloid-lineage leukemia gene at the 11q23 translocation breakpoint [14, 15]. Blast cells or atypical myeloid cells are the dominant cell type of acute myeloid leukemia and tend to appear as monotonous and homogeneous population throughout the peripheral smear. Nuclei are round to oval and sometimes irregular, chromatin is likely to be evenly dispersed, and nucleoli are multiple but potentially inconspicuous. Despite these suggestive histological characteristics, histochemistry and immunohistochemistry are generally required for confirmation of leukemia whether lymphoblastic or myeloid, in addition to examinations of peripheral blood and bone marrow. Congenital leukemia has a poor prognosis with an overall survival rate of only 20% at 2 years of age [6, 14]. Bad prognostic indicators include marked Leukocytosis, Massive hepatosplenomegaly, CNS involvement, Thrombocytopenia, Hypogammaglobulinemia, Disseminated Intravascular Coagulation (DIC), Remission induction not achieved by 14 days of age. In Acute leukemia, the treatment outcome is as follows.

- Survival less than 6 months is 5-15 %
- Survival more than 6 months is 10- 20 %
- More than 2 year survival is 70 %.

Conclusion

In conclusion, congenital leukemia is a very rare disorder. The course of congenital leukemia is aggressive and leads to rapid deterioration and death from hemorrhage and infection. Specifically, it is a even more aggressive disease with increased incidence of leukocytosis, massive hepatosplenomegaly. Like in adults chemotherapy may not be of much use in cases of infants due to toxic effects of chemotherapeutic agents which will be more marked in low birth weight babies.

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